UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte LIRONG LIU, ALEX SHLYANKEVICH, and ANAND BAICHWAL

Appeal No. 2005-0416
Application No. 09/970,020

ON BRIEF[1]

Before WILLIAM F. SMITH, ADAMS and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 24-54, which are all the claims pending in the application.

Claim 24 is illustrative of the subject matter on appeal and is reproduced below:

24. An orally administrable pharmaceutical composition comprising a therapeutically effective amount of an immediate release formulation comprising a (-) chiral compound enantiomer or a pharmaceutically acceptable salt thereof; and a controlled release formulation

[1] Appellants waived their request for oral hearing. Paper received March 28, 2005. Accordingly, we considered this appeal on Brief.

> comprising a (+) chiral compound enantiomer or a pharmaceutically acceptable salt thereof and a heteropolysaccharide and polysaccharide gum excipient.

The references relied upon by the examiner are:

Baichwal et al. (Baichwal)	4,994,276	Feb. 19, 1991
Gilbert et al. (Gilbert)	WO 98/40053	Sep. 17, 1998

GROUND OF REJECTION

Claims 24-54 stand rejected under 35 U.S.C. § 103 as being unpatentable over Gilbert in view of Baichwal.

We affirm.

CLAIM GROUPING

According to appellants (Brief, page 3), "[c]laims 24-54 stand or fall together." Since all claims stand or fall together, we limit our discussion to representative independent claim 24. Claims 25-54 will stand or fall together with claim 24. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

DISCUSSION

According to the examiner (Answer, page 3), Gilbert teaches "a bi-layer tablet that has a controlled release and immediate release profile for tramadol."[2] Specifically, Gilbert teaches (page 5, lines 3-9),

> a preferred dosage form for administration of tramadol is one in which (-)-tramadol is in immediate-release form and (+)-tramadol is

[2] Appellants recognize (Brief, page 3), "Gilbert teaches a dosage form having separate portions (e.g., a bi-layer tablet), each portion containing one enantiomer of a chiral drug (e.g., tramadol...). The enantiomers are released from the dosage form at different rates." See also, Reply Brief, page 2.

> in a sustained-, or controlled-release form. In this case, the release rate of the (+)-enantiomer could be controlled in such a way to reduce the adverse side effects of nausea and/or dizziness believed to be associated with that enantiomer.

The examiner recognizes, however, that while "Gilbert teaches that any conventional controlled-release technology can be used to achieve the desired tablet formulation[,] Gilbert does not expressly teach the heteropolysaccharide and polysaccharide gum excipients formulation" required by appellant's claimed invention. Answer, page 3. The examiner relies on Baichwal to make up for this deficiency in Gilbert.

According to the examiner (id.), Baichwal teaches "a free-flowing slow release excipient formulation comprising a heteropolysaccharide ... and a polysaccharide...."[3] In addition, the examiner finds (Answer, page 5), Baichwal "teaches that the excipients system can be used with a wide variety of drugs that are soluble and/or insoluble and that this system is less expensive and easily compressed in the preparation of the tablets."

Based on this evidence the examiner concludes (Answer, page 4),

> It would have been [prima facie] obvious to a person of ordinary skill in the art [at the time the invention was made] to incorporate the free-flowing slow release excipients formulation taught by Baichwal into the bi-layer tablet that has a controlled release and immediate release profile for tramadol taught by Gilbert because Gilbert teaches that any conventional controlled-release technology can be used to achieve the desired controlled release excipients for delivery of an active agent ... [that] is inexpensive to manufacture and can be easily compressed into tablets which eliminates the use of expensive manufacturing equipment.

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[3] Appellants recognize (Brief, page 3), "Baichwal teaches a heteropolysaccharide and polysaccharide gum excipients for controlled release delivery of a drug." See also Reply Brief, page 2.

In response, appellants argue (Brief, page 4), "[n]othing in Baichwal suggests use of the disclosed sustained release excipients in two-part formulations providing separate delivery rates for enantiomers of a chiral drug. Similarly, nothing in Gilbert suggests use of the particular excipients of Baichwal in the disclosed two-part enantiomer formulations." To the extent that appellants are arguing each reference separately, we remind appellants "[t]he test for obviousness is not express suggestion of the claimed invention in any or all of the references but rather what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them." In re Rosselet, 347 F.2d 847, 851, 146 USPQ 183, 186 (CCPA 1965).

Appellants also assert (Brief, page 4), "the [e]xaminer has not pointed out any specific reasons why one of ordinary skill in the art, without the benefit of [a]ppellants' disclosure, would select Baichwal's excipients from the thousands of known controlled release delivery systems for use in the two-part enantiomer formulations of Gilbert." According to appellants (Brief, page 5), "there simply would have been no motivation for one of ordinary skill in the art to select the sustained release excipients of Baichwal for use in the formulation described by Gilbert." In this regard, appellants assert (Brief, page 6),

> Gilbert teaches controlled-release tablets and bi-layer tablets prepared with a particular controlled release excipient, namely, hydroxypropyl methyl cellulose (HPMC). ... The [e]xaminer has not provided any reason why one of ordinary skill in the art would choose to prepare the formulations of Gilbert using any particular undisclosed conventional controlled release technology, rather than simply using HPMC, which Gilbert specifically teaches and exemplifies.

Stated differently, appellants assert (Reply Brief, page 2), "there is no deficiency in the teachings of Gilbert that would motivate one of ordinary skill in the art to seek out an alternative to the disclosed HPMC controlled release excipients for making a two-part formulation."

It is well settled that the suggestion to combine prior art references must come from the cited references, not from the application's disclosure. See e.g., In re Dow Chemical Co., 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988). As we understand appellants' argument, since Gilbert teaches the use of HPMC, there would have been no reason, other than hindsight reconstruction[4], to modify the teachings of Gilbert to use the sustained release excipients of Baichwal. We disagree. Baichwal recognizes the disadvantages of using HPMC as a slow release matrix for a variety of medicaments. See e.g., Baichwal, column 2, line 34 – column 3, line 45.

Specifically, Baichwal disclose (column 2, lines 34-38), "a great deal of attention in the pharmaceutical field has turned to the use of various hydrocolloid materials such as hydroxypropylmethyl cellulose in providing a slow release matrix for a variety of medicaments." Baichwal provides two examples of slow release compositions containing HPMC. See Baichwal's discussion of the Schor and Alderman patents at column 2, line 39 – column 3, line 7. According to Baichwal, (column 3, lines 8-22),

> [t]he carrier bases which provide the slow release profiles in these disclosures can only be compressed into a tablet or a solid dosage form with the aid of other conventional tableting adjuvants such as

[4] See Brief, bridging paragraph, pages 6-7; Reply Brief, bridging paragraph, pages 4-5.

> binders and the like, and therefore contribute only to the slow release aspect of the final solid unit dosage form and not to the tableting aspects. In other words, in each of these disclosures it is necessary for [sic] to first determine the physical properties of the active medicament to be tableted and thereafter proceed through a series of trial and error experiments in order to determine the optimal amount of gums/polymers and other adjuvants to produce the right formulation which is free flowing and which can be compressed to a slow release solid dosage unit. This procedure is time intensive and costly.

Against this backdrop, Baichwal disclose (column 3, line 61 – column 4, line 5),

> [i]t is therefore an object of the present invention to provide a free-flowing directly compressible slow release excipient which can be used for a wide variety of therapeutically active medicaments. ... It is a further object of the present invention to provide a free-flowing directly compressible slow release excipient which is relatively inexpensive to manufacture due to the lack of coatings and expensive equipment.

According to the examiner (Answer, page 4), "[o]ne would be motivated to use the excipients system of Baichwal for the controlled release portion of the bi-layer tablet because[,] ... [inter alia, it] is inexpensive to manufacture and can be easily compressed into tablets which eliminates the use of expensive manufacturing equipment." Thus, notwithstanding appellants' assertions to the contrary (see e.g., Brief, pages 4-6; Reply Brief, pages 4-5), Baichwal expressly discloses the advantages of using a heteropolysaccharide and polysaccharide gum excipients over the use of HPMC. Accordingly, we are not persuaded by appellants' arguments.

On reflection, we find no error in the examiner's finding that the invention of appellants' claim 24 is prima facie obvious over the combination of Gilbert and Baichwal. Accordingly, we affirm the rejection of claim 24 under 35 U.S.C. § 103

as being unpatentable over Gilbert in view of Baichwal. As discussed supra claims 25-54 fall together with claim 24.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

William F. Smith
Administrative Patent Judge

Donald E. Adams
Administrative Patent Judge

Eric Grimes
Administrative Patent Judge

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